REMARKS

The specification has been amended to replace the Sequence Listing as previously filed with the substitute Sequence Listing attached hereto as Exhibit A. Support for this amendment is found in the Sequence Listing as previously filed. Also attached hereto as Exhibit B is a computer readable form ("CRF") of the Sequence Listing.

Pursuant to 37 CFR § 1.821(f), undersigned counsel hereby represents that, upon information and belief, the content of the paper copy and CRF of the Sequence Listing enclosed herewith are the same, and no new matter has been added. Entry of the Sequence Listing is respectfully solicited.

The Specification has also been amended to insert the sequence identifiers from the Substitute Sequence Listing after the corresponding polynucleotide or polypeptide sequence on pages 31 and 40.

Claims 1, 2, 25, 30, and 31 have been amended to recite an "enzyme having alcohol and aldehyde dehydrogenase activity." Support for these amendments is found in original claims 1, 2, and 25 and in the specification at, for example, page 3, lines 18-21. *See In re Gardner*, 177 USPQ 396, 397 (CCPA 1973) and MPEP §§ 608.01 (o) and (l).

Claims 1 and 25 have also been amended to recite a recombinant polypeptide containing an amino acid sequence of "SEQ ID NO: 8," or "amino acid sequences with at least 80% identity to SEQ ID NO: 8." Claim 29 has been amended to recite an amino acid sequence of "SEQ ID NO: 8." Support for these amendments is found in the specification at, for example, page 34, Table 7 entitled *Homologies of*

amino acid sequences among AADHs, lines 14-19, in the Sequence Listing as filed, and in original claims 1 and 25. (*Id.*).

Claim 2 has also been amended to recite "the recombinant polypeptide is a chimeric polypeptide including a combination of at least two amino acid sequences each of said sequences being selected from the group consisting of SEQ ID NO: 5, SEQ ID NO: 8, and amino acid sequences with at least 80% identity to SEQ ID NO: 5, or SEQ ID NO: 8." Support for this amendment is found in the specification at, for example, page 34, Table 7 entitled *Homologies of amino acid sequences among AADHs*, lines 14-19, and in original claim 2. (*Id.*).

Claim 9 has been amended to recite "pSSB103R." Support for this amendment is found, for example, in the specification at, page 36, lines 7-8 and in original claims 8 and 9. (*Id.*).

Claims 30 and 31 have also been amended to recite "a recombinant expression vector comprising a DNA sequence of SEQ ID NO: 4 or DNA sequences which encode a polypeptide with at least 80% identity to SEQ ID NO: 8." Support for these amendments is found, for example, in original claims 7 and 8 and in the specification at, for example, page 5, lines 1-9, page 17, lines 14-25, and Table 7 (page 34, lines 14-19). (*Id.*).

RESTRICTION/ELECTION:

We hereby affirm the election to prosecute the invention of the polypeptide embodied by SEQ ID NO: 8, which includes claims 1-3, 9, 20-22, 25, and 28-31.

OBJECTIONS:

1. Priority

The Examiner apparently objected to Applicants' claim to priority. In making the objection, the Examiner asserted that "[a]cknowledgment is made of Applicant's claim for priority based on European Patent Office (EPO) 96115001.8 filed September 19, 1996. However [the] priority document is absent from the record." (Paper No. 112104 at 3).

The Examiner further stated "[i]t is noted that this application appears to claim subject matter disclosed in prior Application No. 09/470667, filed 12/22/1999 now patented, and to Application No. 08/934,506 now abandoned. A reference to the prior application must be inserted as the first sentence of the specification of this application ...." (*Id.*)

In response, we note that the application transmittal papers for the above-referenced application filed on March 17, 2004 requested that the specification be amended to insert the continuing application data:

> [x] Relation back under 35 USC § 120: Amend the specification by inserting before the first line, the sentence: -- This application is a divisional of U.S. Application Serial No. 09/470,667, filed December 22, 1999, which is a divisional of U.S. Application Serial No. 08/934,506, filed September 19, 1997, now abandoned. --

The application transmittal papers also indicated that a certified copy of the foreign priority document was filed in U.S. Application Serial No. 08/934,506:

> [x] Priority is hereby claimed under 35 USC Section 119 based on Application No. **96115001.8** filed **September 19, 1996** in **Europe**.

a. [x] A certified copy of the priority document is already of record in U.S. Application Serial No. 08/934,506, filed September 19, 1997.

Therefore, it is submitted that Applicants complied with all rules regarding priority under 35 U.S.C. §§ 119 and 120. (*See* REQUEST FOR FILING A RULE 1.53(b) DIVISIONAL APPLICATION at pp. 2-3). For the reasons set forth above, withdrawal of the apparent objection is respectfully requested.

2. Sequence Listing

The Examiner objected to the specification for lack of a proper sequence listing. In making the objection, the Examiner asserted that "[t]he instant specification on page 31, lines 13 and 15, and on page 40, line[s] 24 and 26, present amino acid and nucleotide sequences that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2), but [the specification] fails to comply with the requirements." (Paper No. 112104 at 3).

With a view toward further prosecution, the specification has been amended to replace the existing Sequence Listing with a substitute Sequence Listing that incorporates the amino acid and nucleotide sequences disclosed on page 31, lines 13 and 15 and page 40, lines 24 and 26. The specification has been further amended to insert sequence identifiers after the polynucleotide and polypeptide sequences on page 31 and the polypeptide sequences on page 40.

For the reasons set forth above, withdrawal of the objection is respectfully requested.

§112, SECOND PARAGRAPH REJECTION:

Claims 1-3, 20-22, 25, and 28-31 have been rejected under 35 U.S.C. §112, second paragraph. (Paper No. 112104 at 6).

In making the rejection, the Examiner asserted that in claims 1-3, 20-22, 25, and 28-31 "[i]t is not clear whether the enzyme has the same function as that of the recombinant polypeptides comprised by the enzyme." (*Id.*).

With a view towards furthering prosecution, claims 1, 2, 25, 30, and 31 have been amended as suggested by the Examiner to recite an enzyme "having alcohol and aldehyde dehydrogenase activity." In view of the foregoing amendment, the rejection of claims 1-3, 20-22, 25, and 28-31 is rendered moot. Accordingly, withdrawal of the rejection is respectfully requested.

§112, FIRST PARAGRAPH REJECTIONS:

1. Written Description

Claims 2-3 and 9 have been rejected under 35 U.S.C. § 112, first paragraph, for lack of written description. (Paper No. 112104 at 7-9).

In making the rejection, the Examiner asserted that "[t]he claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." (*Id.*). The Examiner further asserted that "[c]laim[s] 2 and 3 are directed to an enzyme that comprises a combination of, at least two amino acids sequences each of said sequences being selected from the group consisting of SEQ ID NO: 8, SEQ ID NOS: 5, 6, 7 and amino

acid sequences that are at least 80% identical to SEQ ID NO: 8, SEQ ID NOS: 5, 6 and 7." (*Id.*).

The Examiner acknowledged that "[t]he specification discloses, on Fig. 3, expression vectors pSSAB201 and pSSBA201 that encode a chimera comprising genes encoding SEQ ID NO: 8 and SEQ ID NO: 5." (*Id.* at 8). The Examiner asserted, "[h]owever, neither the amino acid and nucleotide structure nor the function of the chimeras encoded by pSSAB201 and pSSBA201 are disclosed." (*Id.*). The Examiner then concluded that the "[p]rovision of pSSAB201 and pSSBA201 is not sufficient to identify even a single representative species of the claimed genus" and "because applicants did not disclose identifying characteristics of claimed genera of chimeric enzymes and thus the methods of their use, one skilled in the art is not convinced that the Inventors were in possession of claimed invention at the time of filing of the instant application." (*Id.* at 8-9).

With a view towards furthering prosecution, claim 2 has been amended to recite a function of the enzyme (*i.e.*, "having alcohol and aldehyde dehydrogenase activity") and to recite SEQ ID NOs: 5 and 8 and amino acid sequences with at least 80% homology to SEQ ID NOs: 5 and 8. And, claim 9 has been amended to recite pSSB103R.

As is well accepted, there is a ***strong presumption*** that an adequate written description of the claimed invention is present in an application as filed. *See In re Werthheim*, 191 USPQ 90, 97 (CCPA 1976); and MPEP §2163(II)(A). Further, an applicant may show possession of the claimed invention by describing it using

descriptive means such as, for example, words, structures, figures, diagrams, tables, and formulas. *See* MPEP §2163(I).

Whether a specification complies with the written description requirement of 35 USC § 112, first paragraph, is a question of fact. *Gentry Gallery Inc. v. Berklin Corp*, 45 USPQ2d 1498, 1502 (Fed. Cir.1998). Moreover, a proper written description analysis requires an analysis of the specification and an understanding of an ordinarily skilled artisan at the time of the invention. *See* MPEP § 2163(II)(A)(2); *see also Wang Labs. v. Toshiba Corp.*, 26 USPQ2d 1767, 1774 (Fed. Cir. 1993). Here, the specification provides ample information detailing the knowledge in the art and demonstrating that the inventors were in possession of the enzyme as claimed.

Here, the construction of chimeric nucleic acid molecules and polypeptides is specifically disclosed in the specification at, for example, Examples 14 and 15 and in Figures 2, 3, 4, 7, and 8. The specification also discloses the enzymatic activity of these constructs (*see*, *e.g.*, Figure 11). Furthermore, the specification discloses in Tables 11 and 12 comparisons of the substrate specificities of, *e.g.*, the claimed polypeptides. Thus, the specification clearly shows that the applicants were in possession of at least the currently claimed chimeric enzymes (*i.e.*, the chimeric enzymes identified as Enzyme A (*i.e.*, SEQ ID NO: 5) and Enzyme B (*i.e.*, SEQ ID NO: 8), as well as chimeric enzymes "with at least 80% identity to" Enzymes A and B). In view of the foregoing, the rejection has been rendered moot. Accordingly, it is respectfully requested that the rejection be withdrawn.

Claim 9 was further rejected under 35 U.S.C. § 112, first paragraph. (Paper No. 112104 at 9).

In making the rejection, the Examiner asserted that "the specification is lacking the description of biologic deposit." (*Id.*). The Examiner acknowledged, however, that "[t]he invention appears to employ a novel gene and plasmid, pSSB103R." (*Id.*). The Examiner then concluded that a deposit of the subject plasmid is required. (*Id.*).

With a view toward furthering prosecution, the Applicant's are in the process of preparing a deposit to be made under the terms of the Budapest treaty. Once such deposit has been made confirmation thereof, including the required averments will be submitted.

2. Enablement

Claims 1-3, 9, 20-22, 25, 28, and 30-31 have been rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. (Paper No. 112104 at 10).

In making the rejection, the Examiner asserted that "the specification ... does not reasonably provide enablement for any amino acid sequence comprising a sequence that has at least 80% identity to SEQ ID NO: 8." (*Id.*). The Examiner acknowledged, however, that the specification is "enabling for the alcohol and aldehyde dehydrogenase of SEQ ID NO:5, 6, 7 and 8 that are in [sic] at least 80% identical to each other." (*Id.*).

Initially, we note that it is the Examiner's burden to demonstrate that a specification is not sufficiently enabling. *In re Marzocchi*, 169 USPQ 367, 369 (CCPA 1971). To carry her burden, the Examiner must identify and clearly articulate the factual bases and supporting evidence that allegedly establish that undue experimentation would be required to carry out the claimed invention. *Id.* at 370.

With a view towards furthering prosecution, claims 1, 2, 25, 30, and 31 have been amended to recite amino acid sequences or DNA sequences which encode a polypeptide that (1) contains SEQ ID NO:8 or a sequence that is 80% identical to it and has alcohol and aldehyde dehydrogenase activity (*i.e.*, claims 1 and 25), (2) that contains SEQ ID NOs: 5 or 8 or sequences that are at least 80% identical to SEQ ID NOs: 5 and 8 and that have alcohol and aldehyde dehydrogenase activity (*i.e.*, claim 2); and (3) that contains the polynucleotide sequence of SEQ ID NO: 4 or encodes an amino acid sequence that is at least 80% identical to SEQ ID NO: 8 (*i.e.*, claims 30 and 31). Table 7 of the specification details the degree of homology between the AADH (Alcohol/Aldehyde Dehydrogenases) of SEQ ID NO: 8 and three other amino acid sequences having AADH activity, *i.e.*, SEQ ID NOS: 5, 6 and 7, which are disclosed throughout the specification. The results in Table 7 demonstrate that a homology of at least 80% was detected:

Table 7. Homologies of amino acid sequences among AADHs.

	Enzyme A	Enzyme A'	Enzyme A"	Enzyme B
Enzyme A	100	_	_	_
Enzyme A'	89	100	_	_
Enzyme A"	85	86	100	_
Enzyme B	83	82	81	100

(See specification at page 34, lines 15-20). The next highest homology between Enzymes A, A', A", and B to enzymes with known alcohol or methanol dehydrogenase activity was in the range of 26 to 31%. (See Specification at page 34, line 20 to page 35, line 4). Thus, the data in Table 7 clearly provides evidence that the Applicants

enabled the full scope of the amended claims by unambiguously identifying a small number of enzymes having highly homologous polypeptide sequences and sharing a common function -- AADH activity. Accordingly, it is respectfully submitted that undue experimentation would not be required to carry out the currently claimed invention.

For the reasons set forth above, the enablement rejection should be withdrawn.

Claims 2-3 have also been rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. (Paper No. 112104 at 12).

In making the rejection, the Examiner asserted that claims 2 and 3 "do[ ] not reasonably provide enablement for an enzyme that comprises a combination of at least two amino acids sequences each of said sequences being selected from the group of SEQ ID NO: 8, SEQ ID NOS: 5, 6, 7, and amino acid sequences that are at least 80% identical to SEQ ID NO:8, SEQ ID NOS: 5-7 or a sequence that is at least 80% identical to SEQ ID NO:8." (*Id.*). The Examiner, however, acknowledged that claims 2 and 3 are "enabling for the plasmid comprising genes encoding SEQ ID NO: 5 and SEQ ID NO: 8 (plasmids pSSAB201 and pSSBA201)."

With a view toward furthering prosecution, claims 1 and 2 have been amended to recite a function of the claimed enzyme, namely alcohol and aldehyde dehydrogenase activity and to recite exclusively SEQ ID NO: 8 or amino acid sequences with at least 80% identity to SEQ ID NO: 8 (claims 1/3) or SEQ ID NOs: 5 and 8 or amino acid sequences with at least 80% identity to SEQ ID NOs: 5 or 8 (claim 2).

We note that the construction of the currently claimed chimeric nucleic acid molecules and polypeptides is specifically disclosed in the specification at, for

example, Examples 14 and 15 and in Figures 2, 3, 4, 7, and 8. The specification also discloses the enzymatic activity of these constructs (*see, e.g.*, Figure 11). Furthermore, the specification discloses in Tables 11 and 12 comparisons of the substrate specificities of the claimed enzymes. Thus, the specification clearly enables the full scope of the currently claimed chimeric enzymes (*i.e.*, the chimeric enzymes identified as Enzyme B (*i.e.*, SEQ ID NO: 8) and Enzyme A (*i.e.*, SEQ ID NO: 5) and at least the chimeric enzymes "with at least 80% identity to" Enzyme B and Enzyme A).

In addition, the structure of the two chimeras can easily be obtained by one skilled in the art from the information disclosed in the specification (*i.e.*, the sequence listing in combination with the Figures and Examples 14 and 15). Thus, the skilled person is not left "without a[ny] further guidance" as asserted by the Examiner.

In view of the foregoing, it is respectfully submitted that the rejection has been rendered moot. Accordingly, withdrawal of the rejection is respectfully requested.

For the foregoing reasons, favorable action on the merits, including entry of the amendments, withdrawal of the objections and rejections, and allowance of all the claims, respectfully are requested. If the Examiner has any questions regarding this paper, please contact the undersigned attorney.

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box. 1450 Alexandria, VA 22313-1450, on May 11, 2005.

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Respectfully submitted,

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